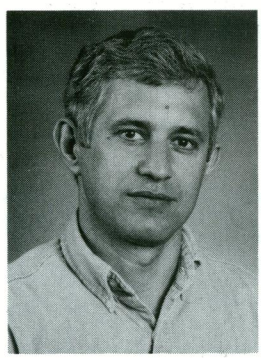
NIEHS News

Getting a Grip on Slippery DNA

Each human cell contains the complete plan and operating instructions for the entire body, in a library composed of 6 billion nucleotides. This information, roughly the equivalent of 1000 volumes of a large college textbook, can be copied in about 8 hours. Amazingly, this process occurs almost perfectly; the error rate inside a human cell may be less than one mistake per genome.

The near-perfection of this process makes the rare errors especially fascinating and significant to scientists. Thomas A. Kunkel, in the NIEHS Laboratory of Molecular Genetics, leads a multidisciplinary team of researchers from various NIEHS labs in pursuit of the secrets of these errors, which researchers have related to genetic diseases including fragile X syndrome, myotonic dystrophy, Kennedy's disease, Huntington's disease, spinocerebellar ataxia type 1, and cancers including colon, gastric, pancreatic, and endometrial. Kunkel notes that these mistakes in the replication process provide useful biological markers in people susceptible to these diseases. The studies also offer insights to the mechanisms through which these genetic diseases and cancers occur and perhaps how they might relate to environmental exposures.

The term "slippery DNA" describes the slippage of one strand of DNA relative to another, the copied strand relative to the template strand. This repositioning causes basepairs to be skipped or added during replication, thus scrambling the genetic information to produce an incoherent message. To help those outside the field better understand the principles at work, Kunkel uses the metaphor of typing. He notes that a typist has the opportunity to correct errors as he or she goes along; likewise, incorrectly copied nucleotides may be corrected as replication is in progress. Later, in the same way that a proofreader catches errors in text and replaces whole words or sentences, the cell "proofreads" its work and can remove incorrectly copied sequences of nucleotides and replace them with corrected ones. Kunkel notes that for a typist to duplicate the feat routinely performed by the cell, he or she would have to type all of the contents of a fairly large personal library with one or zero errors in eight hours.



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Repair man. Thomas A. Kunkel leads a team studying DNA replication errors.

Despite the cell's incredible capability, when errors are not caught and corrected, they give rise to genetic diseases and cancers, although the mechanisms by which these diseases arise have yet to be defined. Further, some genetic errors seem to be amplified in the next generation, as with the retardation associated with the fragile X syndrome, that becomes more severe in successive generations.

Kunkel described the current state of research on slippery DNA as "a ripe opportunity for rapid understanding of biological phenomenon." His review article on the subject appeared in the September 16 issue of *Nature*.

Two New Environmental Health Sciences Centers Funded

The first two Environmental Health Sciences Centers to be established since the development of new center guidelines by NIEHS in 1992 were funded April 1 at Wayne State University in Detroit and the University of Arizona at Tucson. The two new centers bring the number of NIEHS Environmental Health Sciences Centers to 15; the NIEHS centers program also includes five Marine and Freshwater Biomedical Sciences Centers and a Developmental Center, with at least one additional Developmental Center planned. When the two new centers were funded, another three existing centers had their grants renewed: Vanderbilt University, University of California, Berkeley and Massachusetts Institute of Technology.

The center at Wayne State, under the direction of Raymond F. Novak, will focus on molecular and cellular toxicology with human applications. The center will feature research cores on regulation of gene expression, signal transduction, epidemiology, and biostatistics. To support these programs the center maintains facilities for transgenic animals, cell image analysis, immunocytochemistry, *in situ* hybrid-ization, and cell culture.

The center at the University of Arizona at Tucson has formed four interdisciplinary programs: biotransformation, metals, cell injury, and environmental genetics. Center Director Glenn I. Sipes, said that the programs will be supported by five service cores: synthetic chemistry, analytical services, experimental pathology, *in vitro* systems, and biomathematics/molecular modeling. A transgenic animal facility will also be developed to serve the programs.

"The Environmental Health Sciences centers are a national resource for multidisciplinary approaches to problems in human environmental health, and as a group they form a network that fosters communication, innovation, and high-quality research," said Kenneth Olden, NIEHS director. The centers provide a stimulating, multidisciplinary working environment that attracts both established and promising young investigators, according to Olden. They are also a key source of expertise on emerging issues in environmental health and a means for communicating environmental health issues to the public and to elected officials. New NIEHS center guidelines include requirements for community outreach and education programs, which foster involvement with local and regional environmental health issues.

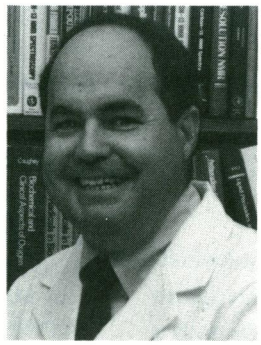
Applications for centers are submitted through the Division of Research Grants at the National Institutes of Health in Bethesda, Maryland, and then assigned to the appropriate institute. Applications received assigned to NIEHS are reviewed on a competitive basis and, if appropriate, approved by the National Environmental Health Sciences Advisory Council, one of the institute's principal governing bodies.

Capturing the Spirit of Science Education

Who will be the environmental health scientists of the future? What makes students develop an interest in science so that they ultimately choose a research career? NIEHS is taking an active role in answering these questions through a variety of education outreach efforts designed to introduce students to the field of environmental science. The outreach program relates experiences that encourage students to consider science careers, and it helps students gain general knowledge about environmental science at the same time.

Years ago, former NIEHS Director David P. Rall noted that along with its basic biomedical research mission, NIEHS is also an educational institution. In those days, the emphasis was on graduate students and postdoctoral scientists and in fact guidelines for NIEHS Environmental Health Sciences Centers grants include education and community outreach requirements at each of the 15 centers nationwide. In recent years, under the

guidance of Director Kenneth Olden, the stimulation of scientific interests in students as young as 5 years old has become a major initiative. Olden notes that only through such efforts can future scientists be recruited, and the informed public to support research be established. The NIEHS Office of Institutional Development held a forum in December 1992 that brought together educators and science professionals to develop ways to educate kindergarten through 12th grade students about the environmental health sciences. The forum served as the basis for a request for applications for grants to develop educational materials to infuse environmental health science concepts into existing curricula. As an outcome of this nationwide grant competition, NIEHS expects to award five or six grants in the summer of 1994.

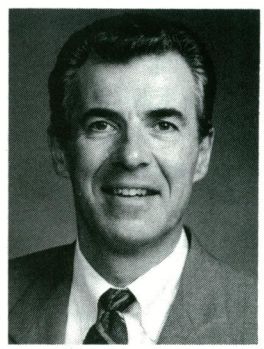


Wayne State U.

Raymond F. Novak

In addition, the NIEHS Divison of Intramural Research supports a program called Summers of Discovery, which provides summer internships that enable students and teachers to work one-on-one with NIEHS scientists. Summers of Discovery offers internships to high school students, college undergraduates, graduate students, and primary through high school faculty, as well as college faculty from traditionally minority and women's colleges and universities. The program includes a seminar series for all participants, weekly lunches with a speaker for faculty participants, and a scientific poster session near the end of the summer at which participants, mentors, and all NIEHS staff can share the successes of the summer.

Another highlight of the NIEHS education outreach is the Environmental Careers Symposium for high school students held on or near Earth Day (this year scheduled for April 20). Sponsored by the NIEHS Division of Intramural Research, the event brings nearly 200 students and teachers to the NIEHS campus for a full day of presentations by a variety of environmental professionals from Research Triangle Park, North Carolina, and surrounding universities. Students have the opportunity to enter an essay contest on an environmental topic with savings bonds as prizes and enjoy a picnic lunch by the institute lake. To reach a wider audience, videotapes with environmental sciences themes are broadcast during school hours on Earth Day by public television and are made available to educators on an ongoing basis. In 1993, the videos produced with NIEHS support by Broadcast Services at North Carolina State University highlighted a number of the career day speakers, featuring their professional work and how they chose science as a career. This year two videos will be produced, a 15-minute film for junior high students showing various approaches (scientific, community action, etc.) to a local environmental problem, and a 30-minute film for high school students depicting the causes and consequences of some environmental exposures.

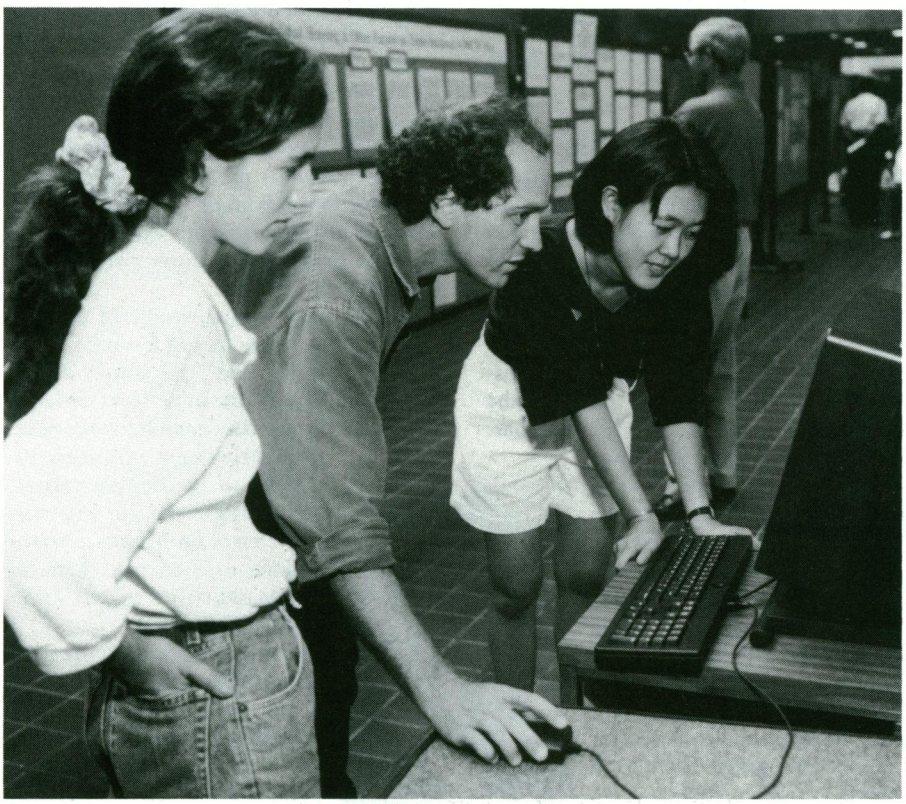


Southwest Env. Health Sci. Center

Glenn I. Sipes

Women and minorities are major targets for science education outreach because U.S. demographics indicate that a growing percentage of scientists must come from these groups if the United States is to supply its share of the world's scientists. As Olden noted in an editorial in *Science*, encouraging minority, and especially African-American, students to take an interest in science involves building an awareness of science as a career within their communities, among their parents, pastors, and teachers. Only through family and community can students receive the social support necessary for their interest in science to move toward a career, Olden said.

Yet another facet of educational outreach is NIEHS scientists and support staff who volunteer to visit classrooms in nearby schools to share their fascination with and knowledge about science with students. To help facilitate and coordinate the education outreach efforts at NIEHS, an education specialist position has been added to the Office of Institutional Development. The education specialist focuses on K–12 programs such as scientist visits to area schools and role model programs in which NIEHS scientists work directly with students to help them understand the importance of science in everyday life and the excitement of science careers. Future plans include teacher-training workshops and a school and community speakers bureau. All of these efforts are designed to improve the community's understanding of environmental health science, increase students' interest in environmental careers, and strengthen NIEHS's visibility in the community.



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What I did last summer. (left to right) Claire D. Sherman and Christopher J. Portier of the NIEHS Statistics and Biomathematics Branch with Sharon Chung, an undergraduate at NCSU, review software written by a Summers of Discovery student.